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Research Article

Analgesic Activity of Sebastiania chamaelea (L.) Muell. Arg.

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Abstract

Background: This study intended to experimentally evaluate the analgesic activity of *Sebastiania chamaelea (L.) Muell. Arg.* which is widely used by folklore and traditional healers in pain relief. The drug is commonly known as 'Bhumi Eranda' among the locals.

Methods: The plant material of *Sebastiania chamaelea (L.) Muell. Arg.* was collected from the fields of Sri Sri College of Ayurvedic Science and Research, Bangalore and preserved as per the standard method. The toxicity studies carried out earlier has proved that, the drug was non-toxic up to 3000 mg/kg body weight. The effective doses were derived as 300 mg/kg (lower) and 600 mg/kg (higher) body weight and the experimental study was conducted. Analgesic screening models used for the study are – Eddy's Hot plate and Tail immersion models. The study was carried out in 4 groups i.e. Control, Standard, Lower dose Kashaya of *Sebastiania chamaelea (L.) Muell. Arg.* and Higher dose Kashaya of *Sebastiania chamaelea (L.) Muell. Arg.* in each model. The activity was compared with a standard reference drug, Tramadol and Diclofenac.

Results: The results were analyzed by using one-way analysis of variance (ANOVA) test followed by Dunnett test to detect the significance of differences between each group and control.

Conclusion: The study helped to conclude, *Sebastiania chamaelea (L.) Muell. Arg.* as an ideal analgesic and supported the traditional claim.

Keywords: Analgesic, Diclofenac, Tramadol

Introduction

After decades of serious obsession with the modern medicinal system, people have changed their outlook about ancient healing systems like Ayurveda, Siddha and Unani. This change might be due to the awareness in public about the severe adverse effects caused by the allopathic drugs. Pain is a complex bio-psychosocial experience and chronic pain requires a multidisciplinary management. Although effective pain management interventions and programs exists, due to multiple failure reasons the prevalence rate of pain is estimated to be 8-60% of the populations.[1] The prevalence of use of analgesics has risen in the recent years despite an improvement in the general health of the population. Pain and discomfort in everyday life are often treated with over-the-counter (OTC) analgesic medications. These drugs are remarkably safe, but serious side effects can occur.[2]

The plant *Sebastiania chamaelea (L.) Muell. Arg.* belonging to Euphorbiaceae family is commonly known as 'Bhumi Eranda'/'Kodiavanakku' among the traditional healers, are used for pain relief in various conditions. 'Kodiavanakku' is used in Vayukshobha chikitsa and antra shola.[3] Leaf decoction of *Sebastiania* in ghritha is considered to be tonic and is applied to the head in vertigo.[4] As per the

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incidence rate of pain, there is an immediate requirement of an ideal analgesic.

Materials and Methods

Collection and Identification of Plant Material

The plant material *Sebastiania chamaelea (L.) Muell. Arg.* (Euphorbiaceae) was collected from the fields of Sri Sri College of Ayurvedic Science & Research, Bangalore and preserved as per the standard method. The taxonomic identity was confirmed by Dr. Shivamanjunatha M. P., Botanist, Department of Dravyaguna, Sri Sri College of Ayurvedic Science and Research, Bangalore. The voucher specimen DGMPS001 was preserved in the Herbarium of Department of Dravyaguna. The plant was thoroughly washed and then dried under shade for one week. The dried material was ground in a mixer grinder and sieved. The powder was stored in air sealed polythene bags at room temperature until further use.

The Pharmacognostic, physicochemical and phytochemical analyses were carried out as per standard protocol.

Models Used in Analgesic Activity

1. **Eddy's Hot plate Method**
2. **Tail Flick Method**

Source of Animals

Healthy Wistar albino rats and Swiss albino mice inbred in Acharya and BM Reddy College of Pharmacy, Bengaluru were selected for the study.

All the Wistar albino rats and Swiss albino mice were subjected to general check-up for sex and weight. Weight of each animal was checked using weighing balance. Identification of animals was done by specific marking with picric acid. The cages were labelled with the number of animals and dosage groups. Animals were housed at ambient temperature and humidity are exposed to 12 hours day and night cycles. Animals did have free access to food and water.

The experimental study was carried out at Acharya and BM Reddy College of Pharmacy, Bengaluru in accordance with the ethical guidelines for animals proposed by Government of India.

Ethical clearance obtained from Department of Pharmacology, Acharya and BM Reddy College of Pharmacy, Bengaluru as per the protocol outlined in publication of the Committee for the Purpose of Control and Supervision of Experiment on Animals standard guidelines (CPCSEA) and approval was obtained from Institutional Animal Ethics Committee (IAEC) with reference no: IAEC/ABMRCP/2016-2017/19.

Dosage Fixation

Acute toxicity studies revealed that there is no toxicity and death of the rats with aqueous and methanolic extracts of *Sebastiania chamaelea (L.) Muell. Arg.* up to 3000 mg/kg body weight even after 21 days.[5] The 1/5th and 1/10th (600 mg and 300 mg) doses were selected for the study.

The dose of standard drug Tramadol was fixed as 13mg/kg body weight of mice for Eddy's hot plate method.[6] The dose of standard drug Diclofenac sodium was fixed as 9 mg/kg body weight of rats for Tail immersion method.[7]

Dosage Form

The Kashaya (decoction) of whole plant of *Sebastiania chamaelea (L.) Muell. Arg.* was freshly prepared and administered daily. The doses were separately calculated considering the weight of rats and mices in each group.

Route of Administration

The drugs were administered orally through metal gavage needle no.24 for rats and mices.

Eddy's Hot Plate Model[8]

Purpose and Rationale

The paws of mice and rats are very sensitive to heat at temperature which are not damaging the skin. The response is jumping, withdrawal of paws and licking of paws. The time until these responses occur is prolonged after administration of centrally acting analgesics, whereas peripheral analgesics of the acetyl salicylic acid or phenyl-acetic acid type do not generally affect these responses.

Procedure

The method originally described by Woolfe and Mac Donald (1944) has been modified by several investigators. The hot plate which is commercially available, consists of an electrically heated surface. This can be copper plate or a heated glass surface. The temperature was controlled from 55°C to 56°C. The animals are placed on the hot plate and the time until either licking or jumping occurs is recorded by stop watch. The latency to the first sign of hind paw licking or jump response to avoid the heat was taken as an index of the pain threshold; the cut-off time was 10 seconds to avoid damage to the paw. The reaction time was calculated and reported.

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Table 1.Grouping of Eddy's hot-plate method

S. No	Grouping	Dosing	Number of mices
1	Control	Vehicle (1 ml/kg, p.o.)	5
2	Standard	Tramadol (13 mg/kg, p.o.)	5
3	Kashaya – lower dose of *Sebastiania chamaelea (L.) Muell. Arg.*	300 mg/kg, p.o.	5
4	Kashaya – higher dose of dose *Sebastiania chamaelea (L.) Muell. Arg.*	600 mg/kg, p.o.	5

Tail Immersion Method[8]

Purpose and Rationale

The method has been developed to be selective for morphine-like compounds. The procedure is based on the observation that morphine-like drugs are selectively capable of prolonging the reaction time of the typical tail-withdrawal reflex in rats induced by immersing the end of the tail in hot water of 55°C.

Procedure

Wistar strain albino rats were used for the study. The rats were immobilized by putting them into individual restraining cages leaving the tail hanging out freely. The animals are allowed to adapt to the cages for 30mins before testing. The lower 5 cm of the tail is marked. This part of tail is immersed in a cup of hot water with temperature 55°C. Within few seconds the rats react by withdrawal of the tail (flicking response). The reaction time was recorded in 0.5s units by stop watch. After each determination the tail is carefully dried. The reaction time is determined after the administration of test substance. The cut off time of the immersion is 15s.

Table 2.Grouping of Tail-immersion method

S. No.	Grouping	Dosing	Number of mices
1	Control	Vehicle (1 ml/kg, p.o.)	5
2	Standard	Diclofenac sodium - 9 mg/kg body weight	5
3	Kashaya – lower dose of *Sebastiania chamaelea (L.) Muell. Arg.*	300 mg/kg, p.o.	5
4	Kashaya - higher dose of dose *Sebastiania chamaelea (L.) Muell. Arg.*	600mg/kg, p.o.	5

Animals Grouped and Caged

Oral Gaviging of Kashaya

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Tail Immersion Method

Eddy's Hot Plate Method

Plate 1.Grouping of animals, dosing and animal experiment models

Statistical Analysis of Experimental Study

Data are expressed as mean ± SEM. The level of statistical significance was taken at P<0.05, using one-way analysis of variance (ANOVA) test followed by Dunnett test to detect the Significance of differences between each group and control.

Results

Results of Kashaya on Eddy's Hot Plate

The result of hot plate indicated that the Kashaya (decoction) showed a significant increase in threshold of pain in a dose dependent manner. Standard drug showed appreciable anti-nociceptive activity throughout the study period. The results are given below in table and graph.

Table 3.Observation of analgesic activity of Eddy's hot plate method

Study duration period	Control group	Standard group Tramadol (13mg/kg, p.o.)	Kashaya of *Sebastiania chamaelea (L.) Muell. Arg.* -. 300mg/kg, p.o.	Kashaya of *Sebastiania chamaelea (L.) Muell. Arg.* - 600mg/kg, p.o.
7 days of treatment	1.4 ± 0.2449	2 ± 0.3162	2 ± 0.3742 **	2 ± 0.2 **

n = 6 animals in each group; Values are mean ± SEM. ** P<0.01, when compared to control.

Results of Eddy's Hot Plate Method

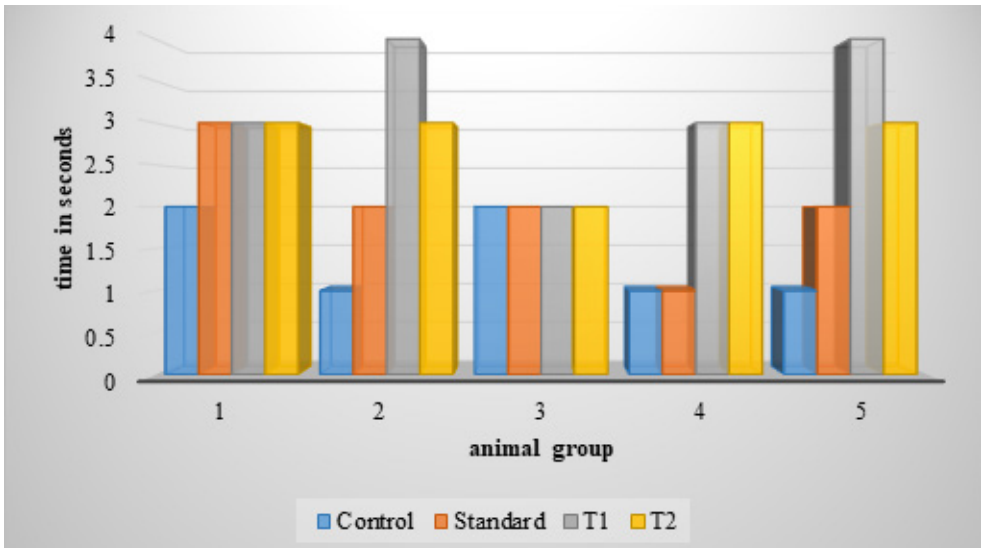

Figure 1.Observation of analgesic activity of Eddy's hot plate method

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The lower dose (300 mg/kg) and higher dose (600 mg/kg) of Kashaya of *Sebastiania chamaelea (L.) Muell. Arg.* showed significant increase in pain threshold with mean values 2 ± 0.374 and 2 ± 0.2 compared to the control group (Figure 1).

Results of Kashaya on Tail Immersion Method

Tail immersion test is also another parameter for analgesic activity. The two doses of Kashaya (decoction) showed significant inhibition with respect to control. The Kashaya showed a significant increase in threshold of pain in a dose dependent manner. Standard drug showed appreciable antinociceptive activity throughout the study period.

Table 4.Observation of analgesic activity of Tail Immersion method

Study duration period	Control group	Standard group Diclofenac (10mg/kg, p.o.)	Kashaya of *Sebastiania chamaelea (L.) Muell. Arg.* -300 mg/kg, p.o.	Kashaya of *Sebastiania chamaelea (L.) Muell. Arg.* – 600 mg/kg, p.o.
7 days of treatment	1.8 ± 0.20	2 ± 0.249	2 ± 0.20 *	2 ± 0.5477

n= 6 animals in each group; Values are mean ± SEM. *** P<0.001, when compared to control.

Results of Tail Immersion Method

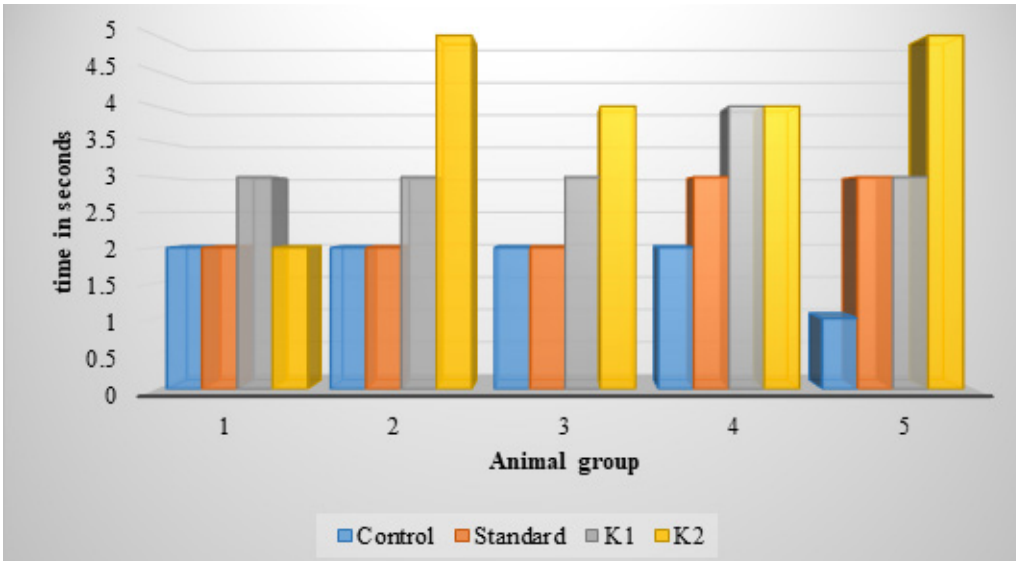

Figure 2.Observation of analgesic activity of Tail Immersion method

The lower dose (300 mg/kg) and higher dose (600 mg/kg) of Kashaya of *Sebastiania chamaelea (L.) Muell. Arg.* showed significant increase in pain threshold with mean values 2 ± 0.20 and 2 ± 0.5477 compared to the control group. When compared between the doses the higher dose -600 mg/kg, p.o. showed suggestive significance than the lower dose (Figure 2).

Discussion

This study is the first report related to analgesic activity of *Sebastiania chamaelea (L.) Muell. Arg.*. Kashaya. The animal models employed for screening of analgesic activity in this study are pain-state models using thermal stimuli which include tail-immersion and hot plate methods. Both methods are useful in illustrating centrally mediated anti-nociceptive responses which focus generally on changes above the spinal cord level. The acute toxicity studies done suggested that drug is nontoxic up to 3000 mg/kg even after 21 days. Kashaya at low and high dose showed significant reduction in pain threshold levels in dose dependent manner.

Eddy's Hot Plate method

Eddy's Hot plate method is one of the promising centrally analgesic models.

Responses such as paw licking and jumping in rats are considered to be supra spinally integrated. Thus, the Kashaya given to inhibit these behaviors on hot plate method indicates that it might be acting at supraspinal level.

Tail Immersion Method

It is known that tail immersion models are the well-established methods for measuring the central analgesic effects of drugs through opioid receptor. In tail-flick model, the Kashaya of *Sebastiania chamaelea (L.) Muell. Arg.* exhibited significant analgesic activity by increasing the

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reaction time of the rats compared to control group at all-time points. The tail-immersion method is based on the observation that Diclofenac-like compounds are selectively able to prolong the reaction time of typical tail-withdrawal effect in rats. This method is also useful in differentiating central opioid-like analgesics from peripheral analgesics.[9]

Analgesic drugs which are centrally acting, elevate pain threshold of animals towards heat and pressure.[9] Therefore, the analgesic effect of the Kashaya on this pain-state model indicates that it might be centrally acting. The brain and spinal cord play an important role in central pain mechanism. The dorsal part of the spinal cord is rich with substance P, endogenous opioids, somatostatin, and other inhibitory hormones which are the targets of pain and inflammation.[10] Although thermal stimuli are used in both tests, the tail-immersion response is due to spinal reflex, while the hot-plate paw-licking response is a supra-spinally integrated response. Present study demonstrated that Kashaya were effective against both the models at 300 mg/kg and 600mg/kg body weight doses which were comparable with standard drugs- Diclofenac and Tramadol.

Narcotic analgesics are active against both peripheral and central pain, while non-steroidal anti-inflammatory drugs inhibit peripheral pain.[11] Our findings suggested that Kashaya may act like narcotic analgesic drugs. The significant increase in pain threshold produced by tests and standard in these models suggests involvement of central pain pathways.

Conclusion

The results support the traditional claim for the use of this plant in the treatment of painful conditions. Acute toxicity studies revealed that there is no toxicity and death of the rats with aqueous and methanolic extracts of *Sebastiania chamaelea (L.) Muell. Arg.* Up to 3000 mg/kg body weight even after 21 days. Kashaya were effective against both the models at 300 mg/kg and 600 mg/kg body weight dose. As per the incidence rate of pain, there is an immediate requirement of an ideal analgesic. The study proved that *Sebastiania chamaelea (L.) Muell. Arg.* is an ideal analgesic compared to Tramadol and Diclofenac with no toxic effects. By experimental evaluation, the drug is proved to be a centrally acting analgesic.

Conflict of Interest: None

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